



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,974	06/20/2001	Mark Laurence Brader	X-11869	9992

7590 11/19/2003

Mark J Stewart  
Eli Lilly and Company  
Lilly Corporation Center/DC 1104  
Indianapolis, IN 46285

EXAMINER

ROBINSON, HOPE A

ART UNIT PAPER NUMBER

1653

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<p align="center"><b>Office Action Summary</b></p>	<b>Application No.</b> 09/868,974	<b>Applicant(s)</b> BRADER ET AL.	
	<b>Examiner</b> Hope A. Robinson	<b>Art Unit</b> 1653	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 September 2003.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 27-47 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 27-47 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☒ All    b) ☐ Some \*    c) ☐ None of:  
         1. ☒ Certified copies of the priority documents have been received.  
         2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
         3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
     a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                             | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____                                    |

### **DETAILED ACTION**

1. Applicant's response to the Office Action mailed May 23, 2003 on September 11, 2003 is acknowledged.
2. Claims 1-26 have been canceled. Claims 27-47 have been added. Claims 27-47 are pending and under examination.
3. The rejection under 35 U.S.C. 112 second paragraph and 102 have been withdrawn. The following grounds of rejection are applicable :

#### ***Claim Objection***

4. Claim 30 and all other claims reciting trade marks such as "Tris and Brj-35" are objected to as the trade mark does not appear in all capital letters (for example TRIS).

Correction is required.

#### ***Specification***

5. The specification is objected to because the appearance of the trademarks "Tris and Brj-35" are not in proper format as the names of the trademark should be completely capitalized (see for example page 3 of the specification).

Correction is required.

#### ***Claim Rejections - 35 U.S.C. § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 27-33 are rejected under 35 U.S.C. 112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 27 and the dependent claims hereto are indefinite because the claim recites "and further comprising one additional amino acid substitution and it is unclear whether the variable X, Y, Z, R1 or R2 contains this additional substitution or if the substitution is a position separate from the listed variables.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 27-29, 31, 33-36, 38, 40-43, 45 and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Jensen et al. (WO 96/20005, July 15, 1996).

Jensen et al. teach a composition containing glucagon-like-peptide-1 (GLP-1), a pharmaceutically acceptable preservative, a tonicity modifier that is glycerol (claims 27, 34 and 41 of the instant application, pages 1-2, 7 and 10 of the reference), compounds having protracted

action and a process for preparation thereof (pages 1-2 of the reference). Jensen et al. disclose that the composition can be in the form of a solution or as part of a gel or foam (claim 27 of the instant application, page 10 of the reference). Jensen et al. teaches a composition having a pH of 8.7 that falls within the range of pH recited in claims 27, 28, 35 and 41-42 (page 8 of the reference). The composition taught by Jensen et al. consists of a pH buffering agent (page 4 of the reference). Jensen et al. also teach that the protracted compositions will spare the diabetics the chore and discomfort of multiple daily injections (see page 1-2). Jensen et al. further teaches GLP-1 compounds and polypeptides comprising 7-34, 7-35 and 7-36 amino acid sequences of GLP-1, for example, the sequence reported in the instant application as SEQ ID NO: 3 (claims 36, page 3). Jensen et al. disclose a sequence with substantial sequence identity to the sequence contained in SEQ ID NO: 2 (27 and 41, page 3). Jensen et al. also teach the above peptide and derivatives of this peptide without eliminating the GLP-1-like activity (page 3). Therefore, the limitations of the claimed invention are met by this reference.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(c), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 27-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andrews et al. (WO 93/25579, December 23, 1993) in view of Jensen et al. (WO 96/20005, July 15, 1996) and Smith et al. (U.S. Patent No. 5,908,830, October 30, 1997).

Andrews et al. teach a composition containing glucagon-like-peptide-1 (GLP-1), salts and derivatives of the claimed protein (claims 27, 34 and 41 of the instant application, pages 1-2 of the reference). Andrews et al. report sequences with a 100% sequence identity to SEQ ID NOS: 2 -3 of the instant application. The composition taught by Andrews et al. consists of a pH buffering agent (see pages 1 and 10 of the reference). Andrews et al. also teach the above peptide and derivatives of this peptide without eliminating the GLP-1-like activity and a method of enhancing insulin action. Although, Andrews et al. does not teach the pH range recited in the claims, Jensen et al. teaches a pH that falls within the claimed range.

Jensen et al. teach a composition containing glucagon-like-peptide-1 (GLP-1), a pharmaceutically acceptable preservative, a tonicity modifier that is glycerol (claims 27, 34 and 41 of the instant application, pages 1-2, 7 and 10 of the reference) and a process for preparation thereof (pages 1-2 of the reference). Jensen et al. disclose that the composition can be in the form of a solution or as part of a gel or foam (claim 27 of the instant application, page 10 of the reference) Jensen et al. teaches a composition having a pH of 8.7 which falls within the range of

Art Unit: 1653

pH recited in claims 27 and 41 and GLP-1 (7-34, 7-35 and 7-36), see pages 2, 8 and Example 4 of the reference). The composition taught by Jensen et al. consists of a pH buffering agent (page 4 of the reference). Jensen et al. also teach that the protracted compositions will spare the diabetics the chore and discomfort of multiple daily injections (see page 1-2). Jensen et al. further teaches GLP-1 compounds and polypeptides comprising the formula I: His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Lys, the sequence reported in the instant application as SEQ ID NO: 3 (page 3). Jensen et al. also disclose a sequence with substantial sequence identity to the sequence contained in SEQ ID NO: 2 (page 3). Jensen et al. further teaches the above peptide and derivatives of this peptide without eliminating the GLP-1-like activity (page 3). Jensen et al. disclose a composition comprising water, a pH buffering agent, an osmotic pressure controlling agent or other ancillary agents (page 4), thus a surfactant such as Brij 35 could be considered as one such ancillary agent as it is well known in the art that this prevents turbidity and surfactants are buffer additives (claims 31-32, 38-39 and 45-46). Moreover, Brij 35 is known in the art as a very good nonionic surfactant. In-so-far-as Andrews et al. and Jensen et al. do not explicitly teach the use of TRIS, Smith et al. discloses the use of TRIS (claims 30, 37 and 44) buffer in a combination therapy for the treatment of diabetes using for example, glucagon agonists (see abstract and columns 6 and 16).

Therefore, it would have been obvious to one of skill in the art to arrive at the claimed invention as a whole because the combined teaching of Andrews et al., Jensen et al. and Smith et al. results in the claimed invention of a shelf stable solution formulation comprising glucagon-like-peptide-1 (GLP-1), a pharmaceutically acceptable preservative, a tonicity modifier, and a

process for preparation thereof for the treatment of diabetes. One of skill in the art would be motivated to combine the teachings of the references as the references aim to treat diabetes utilizing glucagons and Jensen et al. teach that there is a need to provide a composition that will spare the diabetics the chore and discomfort to multiple daily injections. Thus, the claimed invention as a whole is *prima facie* obvious.

10. Applicant's response filed September 11, 2003 has been considered. The arguments presented on pages 6-8 stating that the rejections of record under 35 U.S.C. 102 and 103 should be withdrawn are so noted, however, the rejections above have been made. Note that based on applicants amendments to the claims the rejection under 35 U.S.C. 102 has been amended, however, the rejection that applied the Andrews et al. reference has been withdrawn. Note also that a new ground of rejection under 35 U.S.C. 103(a) has been instituted and the rejection of record has been withdrawn.

Applicant states that the Jensen et al. reference is not relevant because the reference results in a gel and the instant application claims have been amended to recite a solution. This argument is not persuasive because Jensen et al. teach that the formulation can be a solution, gel or foam. Thus, the rejection of record remains under 35 U.S.C. 102. Note that the Jensen et al. reference has been combined under 35 U.S.C. 103 with the Andrews et al. and Smith et al. references to rectify the deficiencies pointed out by applicant. The above rejection sets forth the reasons why one of skill in the art would be motivated to combine the teachings of the references and why the references render obvious the claimed invention.



***Conclusion***

11. Applicant's amendment necessitated the new/modified ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. No claims are presently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope Robinson whose telephone number is (703) 308-6231. The


Art Unit: 1653

examiner can normally be reached on Monday and Wednesday-Friday from 9:00 am to 5:30 pm (EST).


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S.F. Low, can be reached at (703) 308-2923.

Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted by facsimile transmission. The official fax phone number for Technology Center 1600 is (703) 308-4242. Please affix the examiner's name on a cover sheet attached to your communication should you choose to fax your response. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

Hope Robinson, MST 

Patent Examiner

  
KAREN COCHRANE CARLSON, PH.D.  
PRIMARY EXAMINER